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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PENG, BO	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/482,682	VON SEGGERN ET AL.	
	Examiner	Art Unit	
	Bo Peng	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 7/5/06.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1,4-8,10,11,14-18,20-23,41,47,69,95 and 97-101 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) 5,10 and 18 is/are allowed..

6)☒ Claim(s) 1,4,6-8,11,14-17,20-23,41,47,69,95 and 97-101 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is in response to the amendment filed 5 July 2006. Claims 5, 14, 18, 69, 95 and 97 have been amended. Claims 1, 4-8, 10, 11,14-18, 20-23, 41, 47, 69, 95, and 97-101 are pending, and are considered in this Office action.

Rejection under 35 U.S.C. 112, second paragraph

2. The rejection of claim 5 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, **is withdrawn** in view of the amendment to the claim.

3. The rejection of claims 1, 100 and 101 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, **is maintained**.

4. Claims 1, 100 and 101 have been rejected as being indefinite because the limitation of claims 100 and 101 is outside of the scope of claim 1 in previous Office actions.

5. Applicant argues that claims 100 and 101 make reference to SEQ ID NO: 8, which is correspond to the sequence of pCLF that comprises an Ad2 leader sequence and an Ad5 fiber sequence as evidenced by paragraph 278 of the published version of the instant application; US Patent Pub. NO. 20030157688 (Remarks, last paragraph, p.9 to 1st paragraph, p.10).

6. First, Applicant's information about pCLF is inaccurate, or at least inconsistent with the description in paragraph [278] of the instant specification. Paragraph [278] recites as follows:

[0278] To enhance expression of fiber protein by the constitutive CMV promoter provided by the pcDNA vector, a BglII fragment containing **the tripartite leader (TPL) of adenovirus type 5** was excised from pRD112a (Sheay et al., BioTechniques, 15:856-862 (1993) and inserted into the BamHI site of pCDNA3/Fiber to create the plasmid

pCLF having 7469 bp, the plasmid map of which is shown in FIG. 4. The adenovirus tripartite leader sequence, present at the 5' end of all major late adenoviral mRNAs as described by Logan et al., Proc. Natl. Acad. Sci., USA, 81:3655-3659 (1984) and Berkner, BioTechniques, 6:616-629 (1988), also referred to as a "partial TPL" since it contains a partial exon 1, shows correspondence with the Ad5 leader sequence having three spatially separated exons corresponding to nucleotide positions 6081-6089 (the 3' end of the first leader segment), 7111-7182 (the entire second leader segment), and 9644-9845 (the third leader segment and sequence downstream of that segment). The corresponding cDNA sequence of the partial tripartite leader sequence present in pCLF is listed in SEQ ID NO: 8 bordered by BamHI/BglII 5' and 3' sites at respective nucleotide positions 907-912 to 1228-1233 (emphasis added)

According to paragraph [278] of the instant specification, pCLF comprises an Ad5 leader sequence and an Ad5 fiber sequence, not an Ad2 leader and an Ad5 fiber.

7. Secondly, Applicant's argument is not relevant to the rejection because according to the description of paragraph [278] of the instant specification, all TPL exons comprised in SEQ ID NO: 8 of claims 100 and 101 are from Ad5, not from different adenoviruses as required by claim 1, while claim 1 requires exons of TPLs being from different adenoviruses. Thus the limitation of claims 100 and 101 is outside of the scope of claim 1.

8. The rejection of claim 14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, **is withdrawn** in view of the amendment to the claim.

9. The rejection of claim 69 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, **is maintained**. Cell lines 293, A549, W163, Vero and an epithelial cell line do not meet the limitation of the packaging cell line of claim 14, because they do not contain either SEQ ID NO: 32 or SEQ ID NO: 26.

10. The rejection of claim 97 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, **is withdrawn** in view of the amendment to the claim.

Rejection under 35 U.S.C. 112, first paragraph, written description

11. The rejection of claims 1, 4, 6-8 and 11 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement, **is maintained**.

12. Applicant states: "The guidelines for determining compliance with 35 U.S.C. 112 note that the written description requirement for a claimed genus may be satisfied through sufficient description representative number of species by actual reduction to practice, reduction to drawings, or disclosure of relevant identifying characteristics, i.e., structure or other physical and/or properties, by functional characteristics coupled with a known or disclosed correlation bet function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus" (Remarks paragraph 3, p. 8).

13. Applicant then argues specifically that Paragraph [0156] of the published version of the instant specification specifically states that "preferably the TPL exons are from Ad2, Ad3, Ad5, Ad7 and the like, however, they may come from any Ad serotype, as described herein." Hence, one of ordinary skill in the art would be informed by the teachings of the specification, as to how to make an isolated nucleic acid molecule which contains an Ad species other than Ad and which comprises TPL exons from different adenoviruses, cording to claims 1, 4-8 and 11.

14. In response, the guidelines for determining compliance with 35 U.S.C. 112 cited by Applicant are accurate. However, Applicant's argument is not convincing because the instant

specification does not meet the guidelines for determining compliance with 35 U.S.C. 112 for following reasons:

15. Claims 1, 4, 6-8 and 11 read on an isolated nucleic acid molecule comprising an adenovirus TPL, wherein the exons are from different adenoviruses. Since there is no limitation to different adenoviruses, the scope of claim 1 encompasses an isolated nucleic acid molecule comprising a TPL, wherein the exons are from different adenoviruses any strains, species, known and unknown adenoviruses. Although applicant has disclosed a nucleic acid contains Ad5-TPL in the specification, Applicant has not disclosed a single hybrid TPLs from different Ad strains "by actual reduction to practice, reduction to drawings, or disclosure of relevant identifying characteristics, i.e., structure or other physical and/or properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus" according to the guidelines for determining compliance with 35 U.S.C. 112 stated by Applicant.

16. Moreover, as indicated in the specification, there are at lease more than 47 human adenoviruses and more of other species. The genome sequences of a vest majority of adenoviruses are unknown in the art. Neither wild type TPLs of a vest majority of adenoviruses nor their hybrid TPLs are well known in the art as Applicant asserted. Thus, the sufficient description representative number of species of claimed hybrid TPLs from different adenoviruses by actual reduction to practice is necessary to satisfy the written description requirement. Although applicant has disclosed a nucleic acid contains Ad5-TPL, which is well known in the art, in the specification, Applicant has not disclosed a single TPL comprising exons from

different Ad strains, which are not well known in the art, to support all TPL combinations of different Ad strains and species as broadly claimed. Consequently, while the skilled artisan would reasonably conclude Applicant was in possession of Ad5-TPL, there is no indication that Applicant was in possession of all undefined Ad-TPLs of different strains and species as broadly claimed.

17. The rejection of claim 18 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement, **is withdrawn** in view of the amendment to the claim.

18. The rejection of claims 14-17, 20-23 and 69 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement, **is maintained**.

19. Applicant argues that the specification states the constructs and methods of the present invention will support the design and engineering of chimeric viral vectors which express amino acid residue sequence derived from two or more Ad serotypes in paragraph [0016], such as from serotypes 1, 2, 5 or 6; for example Ad37 (subgroup D) paragraph [0021], as well as inducible promoter in Paragraph [0049] (Remarks, paragraphs 2 and 3, p.12)

20. Applicant's argument is fully considered, but found not persuasive for following reasons: First of all, the description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."

21. Specifically, since the claims 14-17, 20-23 and 69 do not define what strains of Adenoviruses and what structure proteins are, the scope of the claims encompasses all cell lines that can package any deficient Ad vectors of any strains and species. As described in the specification, there are at lease more than 47 human adenoviruses and more of other species. Since the adenoviruses genus has a substantial variance, Ad packaging cell lines are strain-specific to package Ad genomes. The disclosure must describe a sufficient variety of species of Ad packaging cell lines to reflect the variation within that Ad genus. See MPEP § 2163. In the specification, Applicant has disclosed a few cell lines that express Ad5 or Ad5/3 fiber proteins for packaging human Ad5 based vectors, but has not disclosed sufficient species of Ad cell lines that can complement all deficient Ad vectors of different strains and species to support the broadly claimed genus of Ad packaging cells. The generic description in paragraph [0016] and [0021] of the instant specification is not sufficient to describe a sufficient variety of species of Ad packaging cell lines to reflect the variation within that Ad genus. The instant specification fails to provide sufficient descriptive information about the Ad packaging cells that can complement all deficient Ad vectors of different strains and species, such as definite structural features, specific Ad proteins expressed and function capabilities of such packaging cell lines.

22. Moreover, the specification has disclosed a CMV promoter, which is well known in the art, but has failed to describe any specific inducible promoters, which are not well known in the art of Ad vector and packaging.

23. Consequently, there is no indication that Applicant was in possession of an Ad packaging cell line that can complement all deficient Ad vectors of any strains or species and any Ad cell lines that contain inducible promoters as broadly claimed.

24. The rejection of claims 41, 47, 95 and 97-99 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement, **is withdrawn** in view of Applicant's argument.

25. The rejection of claims 5 and 18 under 35 U.S.C. 112, first paragraph for failing to comply with the enablement requirement, **is withdrawn** in view of the amendment to the claims.

Rejection under 35 U.S.C. 112, first paragraph, enablement

26. The rejection of claims 1, 4, 6-8, 11, 14-17, 20-23, 41, 69, 95 and 97-101 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement, **is withdrawn in part, and maintained in part**. The aspect that is withdrawn is lacking enablement due to a lack of deposit of the packing cell lines recited in the claims in view of Applicant's argument.

27. The aspect that **is maintained** in claims 14-17, 20-23, 41, 69, 95 is that the specification, while being enabling for Ad packaging cell line 293, 211, 211A to package Ad5 based vectors, does not reasonably provide enablement for A549, W163, Vero and all other unspecified cell line to package Ad defective vector.

28. Applicant argues that the specification teaches one of skill in the art how to make and use A549, W163, Hela vero and other uncharacterized cell line as set forth for example in paragraphs [0144] and [294].

29. Applicant's argument is not convincing for following reasons: A viral package cell line is designed to complement a specific deficient viral vector in order to package the deficient vector

into a virus particle. A549, W163, Hela, Vero, and all other uncharacterized cell lines are incapable of packaging deficient Ad vectors of claim 21 because they do not provide any Ad proteins that are required for packaging the deficient Ad vectors.

30. Moreover, Ad packaging cell lines are strain-specific. While 293, 211 and 211A are able to package an Ad5-based Ad deficient vector, the specification has not shown that they can also be used to package any deficient Ad vectors of different strains and species. Since the limitation in claim 14 clearly covers very broad range of packaging cells that can package all deficient Ad vectors of different strains and species, in view of the empirical and unpredictable nature of the invention with regard to development of packaging cells for all Ad viruses, and lack of guidance and working examples in the specification, one skilled in the art cannot use 293, A549, W163, Hela, Vero, 211, 211A and all other uncharacterized cell lines to package all deficient Ad vectors of any strains and species without undue experimentation.

31. The aspect that **is maintained** in claims 1, 4, 6-8, 11, 100 and 101 is that the specification, while being enabling for Ad5 TPL, does not reasonably provide enablement for other TPL of different adenoviruses. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

32. Applicant argues that the specification exemplifies to one of skill in the art how to make and use TPLs from Ad2 and Ad5. As set forth above, pCLF comprises an Ad2 leader sequence and an Ad5 fiber sequence. The corresponding cDNA sequence of the partial tripartite leader sequence found in pCLF listed in SEQ ID NO: 8 (See paragraph 278 of the published version of

the instant application US Patent Pub. No. 20030157688). Therefore, examples of every possible TPL need not be required in order to meet the standard of enablement (Remarks, paragraph 4, p. 15).

33. Applicant's argument is not relevant because (1) pCLF comprises only Ad5 TPL exons, not TPL comprising different exons from different Ads (see paragraph [246] of instant Application and the discussion set forth in paragraph 6 of instant Office action); (2) "pCLF comprises an Ad2 leader sequence and an Ad5 fiber sequence" does not exemplify a combination of TPL exons from different Ads as claimed in claim 1. Finally, the instant specification does not exemplify any hybrid TPL exons from different Ads as suggested by Applicant.

34. Again, since there is no limitation to different adenoviruses, the scope of claim 1 encompasses an isolated nucleic acid molecule comprising a TPL, wherein the exons are from different adenoviruses any strains, species, known and unknown adenoviruses.

The state of art is that genome sequences of a vest majority of adenoviruses are unknown, neither their TPLs. Only a few strains of Ad genomes were sequenced and partially characterized at the time of the instant application was filed. TPL sequences vary in different adenoviruses. A secondary structure is formed within Ad TPL to facilitate the translation of viral mRNAs (Zhan et al 1989). Since TPLs are strain-specific, precise sequences of exons and introns of different Ads and their location in their genomes are required to make claimed nucleic acid molecule comprising TPLs from different adenovirus. Neither the instant specification nor the prior art has provided guidance how to make nucleic acid molecules comprising TPLs of different adenoviruses without knowing their sequences. The specification does not provide any real

hybrid TPLs comprising exons from different Ads can still maintain their secondary structure to facilitate translation reactions.

35. Since the limitation in claim 1 clearly covers a very broad range of adenoviruses, considering the state of the art as discussed above and the high unpredictability and lack of guidance and working examples in the specification, one skilled in the art cannot practice the claimed invention without undue experimentation.

Rejection under 35 U.S.C. 103(a)

36. The rejection of claims 6-8 under 35 U.S.C. 103(a) as obvious over Logan as evidenced by Clark, further in view of Curiel (US 5,871,727) **is withdrawn** in view of Applicant's amendment.

Remarks

37. Claims 1, 4, 6-8, 11,14-17, 20-23, 41, 47, 69, 95, and 97-101 are not allowed.

38. Claims 5, 10 and 18 are allowable.

39. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, Ph.D. can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Bo Peng, Ph.D.
September 13, 2006

MARY E. MOSHER, PH.D.
PRIMARY EXAMINER